

**CERTAIN MEDICAL ASPECTS OF RECURRENT MALIGNANT TUMORS.**

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It is frequently the experience of physicians to see a patient from whom a malignant growth has been removed long before, in whom recurrence has taken place, not at the site of operation, not in the shape of visible and palpable tumor masses in distant parts of the body, but with symptoms that resemble those of a so-called medical or internal disease as distinguished from the external or surgical, *i. e.*, operable affection. To such manifestation the term medical or non-surgical recurrence may be applied, though such a use of the term recurrence is open to criticism, because in the strict sense it is not a recurrence. The distant foci of tumor cells were already established at the time of operation, though dormant, but are now aroused into activity; or tumor cells slipped into the circulation during the manipulation of the operation and, lodging in distant parts, later as metastases, produce the symptoms to which reference has been made. So, also, these are really borderland cases and not strictly medical.

It is the purpose of this paper to call attention in a brief and practical manner to some of the very varied clinical manifestations of such recurrences as they might be met with in general practice. It is hoped that it may contain some helpful hints as to diagnosis.

Four things are likely to stand in the way of the early and easy recognition of the presence of these so-called medical recurrences: (1) The fact that there is no recidivation at the site of operation; (2) that no tumor mass can be made out in other parts of the body; (3) the long duration of time that may have elapsed since the operation, during which time the patient has apparently been healthy, and (4) the fact that the symptoms are not those commonly associated with tumor, but rather those of some other, often a so-called medical, condition.

The first three stumbling-blocks to diagnosis should be easily avoided by remembering that they are by no means exceptional, and should not be given much weight in excluding the presence of neoplasm. The thoroughness with which surgeons today remove tumors, *e. g.*, of the breast, makes recurrence *in situ* comparatively rare when an early diagnosis has made an early operation possible. A soft, pliable scar with no regional glandular involvement proves the conscientious carefulness with which the surgeon has done his work, but does not exclude metastases elsewhere. And these metastases need not be large masses in order to produce symptoms. We are familiar with the large tumor in the abdomen that comes

after the removal of a sarcomatous testicle; or the indurated mass found in the pelvis on rectal or vaginal examination, which represents the recurrence after the operation for carcinoma of the uterus or rectum; or the enlarged liver that appears after the removal of a melanotic sarcoma of the eye or a cancerous pylorus. But failure to find such frankly neoplastic deposits should not cause us to rule out the presence of smaller and hidden ones. Nor should a lapse of many months or even two or three years throw us off our guard and cause us to feel secure against return of malignant growth. Longer periods than this may elapse before there is evidence of metastatic activity. I have known eight years to pass after the removal of a carcinomatous breast before the patient succumbed to metastases which were evident only at autopsy.

The fourth difficulty is one not so easily surmounted. At times it is only by careful exclusion of other diseases, or by patiently tracing some atypical symptom or sign to its malignant source, that a correct diagnosis is made. And often this diagnosis can be only a presumptive one.

Some of these clinical features are worthy of special consideration. Among them are nervous symptoms, which may often accurately resemble those of other diseases. Thus pain in the lumbar, sacral, and gluteal region may readily pass for sciatica. It may, in fact, be genuinely sciatic in origin, a nodule pressing on this nerve or tumor cells invading the nerve sheath. At times, however, a careful examination will show a tenderness that is in the sacrum or the lumbar vertebrae, rather than in the nerve itself. It represents a bone metastasis, with perhaps pressure on the nerve roots as they leave the vertebral canal. One of the confusing features in some of these cases of severe lumbar and sciatic pains (and the same is true of Pott's disease and the spondylitis of typhoid) is the fact that the patients often become "nervous," sleepless, complaining, even hysterical, craving morphin, and the thought of the whole trouble being functional, a sort of railway-spine affair may be entertained. The true nature of the lesion may be revealed only when a pressure paraplegia supervenes. Neuralgic pains in other parts of the body, as in the intercostal nerves or in the scalp, may have their origin in deposits of tumor in bone. That certain tumors, as of the breast, thyroid, prostate, and adrenal, are prone to form metastatic deposits in bone is well known. No pain, therefore, occurring in a patient who has been operated upon for a malignant growth, and especially a growth in one of these organs, should be passed as due to simple neuralgia until careful search has been made to exclude bone metastases. At times an irregularity or swelling of the surface of the bone over the spot of tenderness will be helpful. The bone may crackle or fracture under even light pressure, as I have seen happen in the case of a rib. The roentgenogram may show focal changes in the bone and

myelocytes or other blood change may be suggestive of involvement of the marrow in disease. A somewhat confusing feature is the disappearance of pain over the site of a bone deposit and the variation in tenderness that may materially change from day to day. Perhaps variation in circulatory conditions may explain these changes; and one may conceive of the tumor mass breaking through a surrounding shell of bone, the pain lessening as the pressure is relieved. Cerebral symptoms may be variable, *e. g.*, symptoms of brain tumor from metastatic deposits. In one case, months after an amputation of the breast, in which local recurrence had taken place, a sudden plugging of the central artery of the retina occurred, presumably by tumor cells.

Another group of symptoms, often confusing, concerns the respiratory tract. Long after the operation a patient may be taken with a cough, and then develop what seems to be an ordinary bronchial catarrh. The cough persists, dyspnea appears, and there is some cyanosis. The sputum is scanty, or it may be mucus or blood-tinged. Rales, dry and moist, may be heard in various parts of the chest, and possibly here and there is made out an area of harsher respiration, or perhaps a spot of dulness. There is little or no fever as a rule. Dyspnea may increase and the respiration grow hurried. There is some loss in weight. It is necessary for one to see an autopsy on only one of these cases, with the lung riddled with small or larger tumor nodules, to be able to understand how the condition resembles clinically miliary tuberculosis. Of course, larger masses may produce symptoms that are more clearly those of tumor. These larger tumors are more easily recognized, or at least suspected, from the predominance of pressure symptoms. The Roentgen rays in both types of thoracic metastases may be of material help in diagnosis.

Another metastatic phenomenon, often a late one, and often the first sign of failing health after the operation, is pleural effusion. Local pain with friction rub may clearly indicate involvement of the pleura; or dyspnea and dry cough may lead to an examination of the chest and a pleural cavity may be found to contain a large amount of fluid, no pain worthy of the patient's notice having been complained of. At times pain, some fever, or rapidly developing dyspnea will make the process resemble tuberculous pleurisy; or even a pneumonia may be thought of if bronchial breathing be detected in some part of the affected side. Rheumatic, tuberculous, and traumatic origin for the pleural fluid, as well as the ordinary causes for hydrothorax, must be excluded as accurately as possible. Bloody fluid obtained by exploratory puncture, the fluid perhaps containing tumor cells or large multinucleated cells, with mitotic figures, and lacking the lymphocytes and tubercle bacilli of tuberculous fluid, may be of material help. Often the fluid recurs even after repeated tapplings that may be necessary

for the relief of pressure. At times it will disappear. Such a disappearance took place in a remarkable case which I saw of late metastases months after the removal of a malignant syncytioma. Sudden large pleural effusion with pain and some fever followed the carriage into the pleura of the tumor cells. These apparently gravitated to the bottom of the pleura, where a large growth developed, invading the diaphragm and the lumbar vertebra, leading ultimately to paraplegia and death. No tumor mass was ever made out on physical examination during life, and no pelvic recurrence took place. The autopsy revealed the above chain of events.

Pleural fluid, therefore, in one who even years before has had a malignant tumor removed should arouse the suspicion of pleural metastases, nor should the temporary disappearance of this fluid lead to a too confident quieting of this suspicion.

Another remarkable phenomenon was seen in a young man of about twenty years, who consulted his physician for slight temperature, cough, and symptoms suggestive of incipient tuberculosis. A sudden and severe hemoptysis occurred. The acute anemia was extreme and out of all proportion to the amount of blood lost externally. Dyspnea was pronounced. The explanation was found in a hemopneumothorax. The lung had ruptured and a large amount of blood with air was in the pleural sac. Death from anemia seemed imminent, but after many days of delirium, prostration, and fever, due to the absorption of the blood, improvement occurred and the boy returned to his home. The explanation for this odd occurrence was found in a metastatic sarcoma of the lung. Five years before the boy's thigh was amputated for sarcoma of the tibia. No local recurrence. A few months after the pulmonary accident just described the boy died with every evidence of thoracic tumor. I have seen another case of metastasis in the pleura with fluid long after amputation of the leg for sarcoma, and one after removal of the testicle.

Just as a pleurisy, especially an afebrile pleurisy, should in these patients arouse a suspicion of the localization of secondary tumors in that tissue, so an otherwise unexplained ascites should lead to a careful examination for proof of the malignant origin of the abdominal fluid from direct involvement of the peritoneum or pressure on the larger trunks of the portal vein. Bloody or chylous fluid may be significant.

Personally, I have never seen clinical symptoms from involvement of the heart by tumor metastases following operation, though at autopsy symptomless nodules in the myocardium or pericardium are occasionally met with. Nor have I noticed clinically symptoms that could be referred to metastases in the kidney.

One type of disease due to these metastases is characterized chiefly by severe anemia and marasmus. This I have seen in a recurrence after removal of carcinoma of the breast. In this in-

stance symptoms like diabetes insipidus were present for many weeks. While autopsy of the body showed numerous nodules, the brain was not examined. Perhaps here was the tumor that induced the polyuria, by pressure on the hypophysis. In another case a profound anemia much resembling pernicious anemia came on months after an operation for carcinoma of the penis.

Occasionally there is reluctance to accept a diagnosis of post-operative metastasis, because a nodule appearing after the operation in some distant part of the body has for a long time remained stationary in size, or has even at times seemed smaller. This should not, of course, rule out a malignant growth. The glands in the neck that are secondarily carcinomatous, as with primary cancer of the stomach, do not, of necessity, grow rapidly. I have seen a carcinomatous gland in the left side of the neck remain the size of a hickory-nut for a year, its first appearance being a few months after the removal of a breast for carcinoma. This patient had also carcinoma of the vertebra, with later paraplegia.

Every physician knows the danger there is in asking a patient what in the law courts are called leading questions. Unconsciously we may suggest answers to such a patient, or lead the history away from facts that would otherwise be clearly brought out by the patient's unguided recital of the history. But there are times when direct questioning is necessary and where it must be pressed. We know how a patient who fears tuberculosis will dodge and evade a direct answer that seems to him incriminating. One must often push the questions and insist upon definite answers.

Similarly, unless direct questioning is resorted to, one may sometimes fail to learn of the previous operation; the patient may forget to speak about it, or regard it as insignificant, or may be purposely concealing the fact. Even the physician may at times be inclined to underestimate the importance, from a diagnostic point of view, of the removal of a seemingly insignificant pigmented mole, or a "polypus" from the neck of the uterus. And the patient may have been given to understand that the tumor was innocent, though a telephone conversation with the surgeon who operated, or a reference to hospital records, might reveal the malignant character of the growth. A fear of learning the serious nature of the illness may induce a patient purposely to make false or misleading statements regarding previous operations, or to conceal the scars of these from the eye of the examining physician. I well remember a case of left-sided pleural effusion in a woman whose left breast had been removed some time before for carcinoma. The careful doctor had made several examinations of the chest, but through seeming modesty, as became a maiden lady of fifty, the clothing was on the occasion of these examinations always deftly arranged by the patient so that the scar of the operation was covered. Great was the surprise and embarrassment of the doctor as this scar

came into view when, at the consultation, in response to insistent requests, the clothing was removed from the chest. The clue to the nature of the pleural effusion was evident. The possibility that a scar may mean the previous removal of a malignant growth should always be taken into consideration, whether such scar be on the lip, the scrotum; cervix uteri, the breast—in fact, anywhere. An absent eyeball has more than once led to the diagnosis of melanotic sarcoma of the liver.

In conclusion it may not be amiss, after having referred so often to the necessity of a thorough examination of these patients in whom there are obscure postoperative manifestations of malignant tumors, to call attention to the importance of such investigation before operation. A thorough exploration of the pelvis per vaginam and per rectum would sometimes ward off the useless operation for carcinoma of the stomach or breast. Secondary peritoneal tumors, as is well known, may sometimes plainly be made out on rectal examination. Such examination may readily be omitted when there are no pelvic symptoms, and when a palpable tumor of the stomach invites to operation. Unless obstructive or other urgent indications point to removal of the primary growth the detection of secondary deposits will contraindicate the operation. In three cases of hypernephroma I have seen operative removal of the kidney vetoed, once because of a secondary tumor in the brain, another time because of secondary deposits in the lung, and in a third case, the deciding voice being that of the late Christian Fenger, because edema of the leg made growth into the vena cava probable, and autopsy showed this to be the case. In a recent case secondary tumors in the lung decided against removal of a carcinomatous tongue. Percussion, auscultation, and the Roentgen rays all clearly showed the invasion of the chest. Such a warning as this may seem uncalled for. But clinical experience has made me feel that it may not be out of place to speak of these things, for it is often the well-known and commonplace that is forgotten, and that from time to time needs to be brought back to our attention.

### **VALUE OF RADIUM, SUPPLEMENTED BY CROSS-FIRE ROENTGEN RAYS, IN TREATMENT OF MALIGNANCY.<sup>1</sup>**

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MUCH discussion has taken place in regard to the comparative value of radium, mesothorium, and the Roentgen rays in the

<sup>1</sup> Read before the Allegheny County Medical Society, January 19, 1915.